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Concerning the following application:

ATTORNEY DOCKET NO.: 18396/2112

Application of:	Sattelle, et al.	Examiner:	Not Yet Assigned
Serial No.:	10/010,873		
Filed:	December 7, 2001	Group Art Unit:	1632
Entitled:	RECOMBINANT NEMATODE NICOTINIC RECEPTOR AND USES	Conf. No.:	7464

Facsimile No.: 1-703-746-9195
Our Facsimile No.: 1-617-227-4420
Number of pages including cover sheet: 7
Transmitted herewith: Transmittal Letter; Request for Corrected Filing Receipt; Copy of Page 1 of Application; Marked-Up Version of Official Filing Receipt

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Date: June 16, 2004

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Atty. Docket No.: 18396/2112 PATENT

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Brenda M. Woods
Name of Person Faxing

Brenda M. Woods
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Commissioner for Patents
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TRANSMITTAL LETTER

Enclosed for filing the above-identified patent application, please find the following documents:

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The Commissioner for Patents is hereby authorized to charge any fees to Deposit Account No. 16-0085, Reference 18396/2112. A duplicate of this transmittal letter is enclosed for this purpose.

Respectfully submitted,

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Name of Person Faxing Paper

Brenda M. Woods
Signature of Person Faxing Paper

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CORRECTED FILING RECEIPT

Sir:

Applicants request issuance of a corrected Official Filing Receipt for the above-identified patent application. Although at the time of filing a large entity fee was paid, the entity is and has been a small entity. The filing receipt should claim small entity status as noted on the marked up version of the Official Filing Receipt.

In addition, the filing receipt should list the title of the application as "Recombinant Nematode Nicotinic Receptor and Uses" as indicated on page 1 of the Application filed on December 7, 2001 (copy enclosed). Please add to Filing Receipt in your proper manner.

A copy of the official Filing Receipt is enclosed with the corrections highlighted in red and underlined. It is believed that no further fees are due for this application.

Respectfully submitted,

Date: June 16, 2004

Barbara A. Gyure

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/010,873	12/07/2001	1632	870	18396/2112	8	12	2

CONFIRMATION NO. 7464

UPDATED FILING RECEIPT

"OC000000012237637"

29933
PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

Date Mailed: 03/31/2004

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Applicant(s)

David Sattelle, Oxford, UNITED KINGDOM;
Emmanuel Culetto, Orsay, FRANCE;
Howard Baylis, Cambridge, UNITED KINGDOM;

Domestic Priority data as claimed by applicant

This application is a CIP of PCT/GB00/02270 06/09/2000

Foreign Applications

UNITED KINGDOM GB99/13248.2 06/09/1999

If Required, Foreign Filing License Granted: 02/05/2002

Projected Publication Date: 07/08/2004

Non-Publication Request: No

Early Publication Request: No

Small Entity

Title

Recombinant nematode nicotinic receptor and uses

Preliminary Class

514

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Express Mail Label No.: EL326923779US
Date of Deposit: December 7, 2001
Atty. Docket No.: 18396/2112

Recombinant Nematode Nicotinic Receptor and Uses

Introduction

The nematode *C. elegans* has permitted identification and functional analysis of novel genes expressed in the nervous system (Bargmann, 1998). This invertebrate animal provides a highly effective genetic model with which to analyse *in vivo* molecules involved in chemical synaptic transmission (Jorgensen and Nonet 1995; Rand and Nonet 1997; Sattelle 1998). Neuromuscular cholinergic synapses in *C. elegans* have been analysed in detail stimulated by the finding that two major postsynaptic components, acetylcholinesterase (AChE, EC 3.1.1.7) and the nicotinic acetylcholine receptor (nAChR), are targets for widely used anthelmintic drugs. The hydrolytic enzymes AChEs which terminate the actions of ACh are inhibited by carbamates and organophosphates (Massoulié et al 1993). The nAChRs mediate the fast actions of the neurotransmitter ACh. When ACh binds to an nAChR molecule, the receptor molecule becomes transiently permeable to cations (Na^+, K^+, Ca^{2+}). Anthelmintic drugs such as levamisole, pyrantel and morantel are agonists and open channel blockers at native nematode muscle nAChRs (Martin 1996). The studies to date of cholinergic anthelmintic actions on recombinant ACR-16 (=Ce21) homomeric (probably neuronal) nAChRs (Ballivet et al; Raymond et al 1999) do not mimic the actions observed on native nematode muscle nAChRs.

Five polypeptide subunits surround a central ion channel in each nAChR molecule, each polypeptide having four transmembrane regions (M1-4) and a large N-terminal extracellular domain containing residues that form the ACh binding sites (Karlin, 1993; Unwin 1993; Lena & Changeux 1998). These subunits are classified as either α subunits, possessing two adjacent cysteines in loop C of the ACh binding site or non-α subunits, with no such adjacent cysteine motif.

Radioligand binding studies suggest the possibility of a diversity of nAChRs in *C. elegans*. For example, using [^{3}H]*meta*-amino levamisole, a high saturable affinity binding activity has been observed and is regulated in the course of development, the highest binding activity being detected in larval stages (Lewis et